

Glaucoma pick your poison!

COPE 60549-GL

Elliot M. Kirstein, OD, FAAO
Harper's Point Eye Associates
Glaucoma and Diabetes Eye Institute
Cincinnati, Ohio

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financial disclosures

- Alcon, Inc.
- Haag – Streit USA
- Optovue
- Reichert
- Aerie

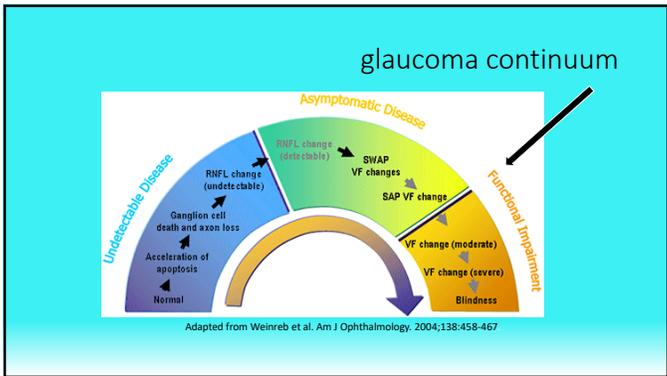
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definition

“The excavation of the disc in glaucoma is not a purely mechanical result of exalted pressure; it is, in part at least, an atrophic condition which, though primarily due to pressure, includes vascular changes and impaired nutrition of the substance of the optic disc... which may possibly progress even though all excessive pressure be removed”.

Priestly Smith 1885

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OD's need to diagnose and treat more glaucoma

- 40,000 OD's
- 8,000 Rx 4 -6 Rx's per year
- 4,000 average 12 – 24 Rx's per year
- Only 2,500 – 3,000 treat with more than one medicine and Rx more than 3 x / month

Paul Karpecki, OD, FAAO

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Sub specialization of ophthalmology

- Cataract
- Cornea
- Refractive
- Retina
- Pediatric
- Neuro
- Oculoplastic
- Glaucoma – end stage

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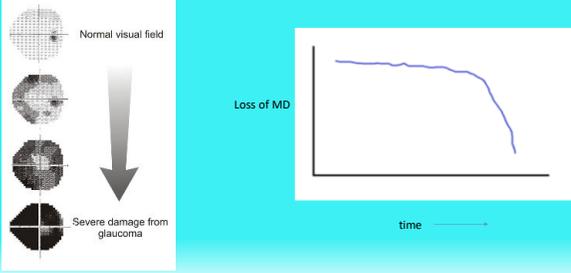
Quality of life

- We want to die young at an old age!



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Velocity and Acceleration of Glaucoma



Normal visual field

Severe damage from glaucoma

Loss of MD

time

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Patients live longer than most doctors predict
 -Kirk Douglas @101

Median age of patient in OHTS:
 56 years (30 year life expectancy)

There is a significant risk of conversion in only 5 years



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“After age 50, I don’t care!”
 (Mother Nature)

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Time to treat?

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When do YOU “chicken out”?

- 21 mm Hg?
- 24 mmHg?
- 26 mmHg?
- 30 mmHg?



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IOP and progression time to treat?

- Australian Blue Mountain Study – IOP 21 mm and over has 4.7 X the risk compared with normal pressure range

Niese, P, Flammer J. Correlations between intraocular pressure, visual field and visual acuity, based on 11 years of observations of treated chronic glaucomas. Int Ophthalmol 3: 31-5, 1980

- Baltimore Eye Study – IOP of 30 mm and over has 38 X greater chance of progression

Sommer A, Titcher JM, Katz J, et al. Relationship between intraocular pressure and primary open angle glaucoma among white and black Americans. The Baltimore Eye Survey. Arch Ophthalmol 109:1090-5, 1991

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Treatment Options

- Prostaglandins
- Alpha Antagonists
- Carbonic Anhydrase Inhibitors
- Beta Blockers
- Miotics
- Rho Kinase Inhibitors
- Surgery

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Prostaglandins the front line

- Uveal – scleral pathway mechanism
- QD dosing
- Safety
- Efficacy
- Cost
- Hyperemia
- Iris pigmentation
- Lash growth
- Loss of orbital fat
- Macular edema
- Consensus - considered front line

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Hyperemia - prostaglandin



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Prostaglandin – iris pigmentation



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Prostaglandin – periorbital fat atrophy



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Lash growth - prostaglandins



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Prostaglandin Preservative Free

- Tafluprost – (Zioptan) Unit dosage
- Latanoprost – preservative free – (XELPROS) new 2019



UK



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Prostaglandins – Brand vs. Generic Study?

- 1) Takes too long?
- 2) Costs too much?
- 3) Too difficult?
- 4) Scarred S—tless about results?

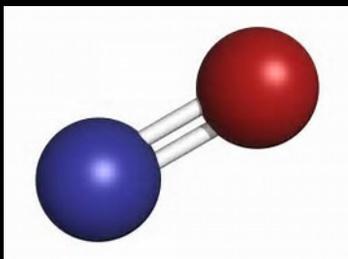
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new toys



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Nitric Oxide (NO)



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Nitric Oxide in Medicine

- Nitroglycerin discovered by the Italian chemist Ascanio Sobrero
- Ascanio also noted that it relieved headaches
- Alfred Nobel – experimented with nitroglycerine and developed dynamite
- Lauder Brunton, a distinguished British physician, had found in 1867 that organic nitrates were effective in relieving pains in angina pectoris
- Alfred Nobel established the prizes in 1895



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NO in non-ocular pathophysiology

- eNOS reduces production of NO which then reduces the production of cGMP.
- cGMP dysregulation plays a role in many human disease process related to vasoconstriction and / or vasospasm

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NO in non-ocular pathophysiology

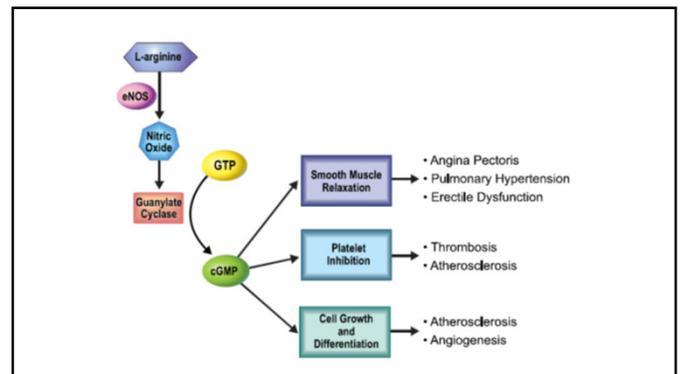
- Angina pectoris
- Pulmonary hypertension
- Erectile dysfunction
- Thrombosis
- Atherosclerosis

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Increasing cGMP levels
treats

- Erectile dysfunction
- Asthma
- Pulmonary atrial hypertension
- Myocardial failure
- Endotoxic shock

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Bausch & Lomb / Nicox
latanoprostene bunod
VYZULTA

- Preclinical studies have shown that NO plays a role in controlling IOP in normal eyes by increasing aqueous humor outflow through the trabecular meshwork and Schlemm's canal.
- Studies have also demonstrated that patients with glaucoma have reduced levels of NO signaling in their eyes, providing a rationale for the therapeutic value of NO-releasing molecules for patients with open-angle glaucoma or ocular hypertension.

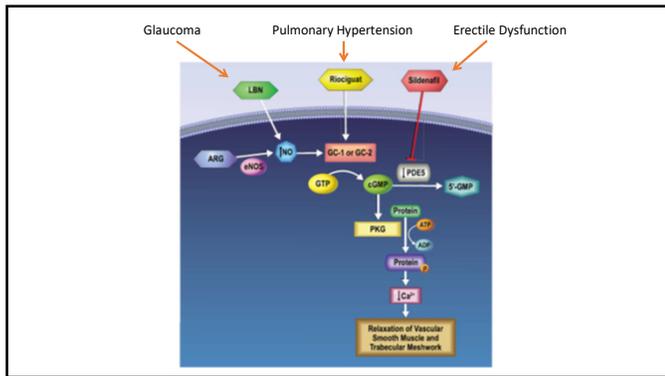
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new and now available

BAUSCH + LOMB



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Nitric Oxide (NO) in the optic nerve

- NO donors decrease vascular resistance by relaxing smooth muscle

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Latanoprostene Bunod 0.024% in Subjects With Open-angle Glaucoma or Ocular Hypertension: Pooled Phase 3 Study Findings

Weinreb, Robert N. MD; Liebmann, Jeffrey M. MD; Martin, Keith R. MD; Kaufman, Paul L. MD; Vittitow, Jason L. PhD
Journal of Glaucoma: January 2018 - Volume 27 - Issue 1 - p 7-15

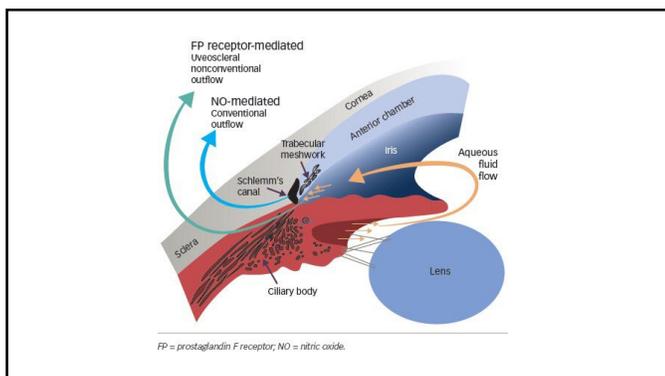
Conclusions: In this pooled analysis of subjects with OAG and OHT, LBN 0.024% qd provided greater IOP-lowering compared with timolol 0.5% bid and maintained lowered IOP through 12 months. LBN demonstrated a safety profile comparable to that of prostaglandin analogs.

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Bausch & Lomb / Nicox - latanoprostene bunod "VYZULTA"

- Showed greater IOP reduction compared with latanoprost, with the differences reaching 1.23 mm Hg
- 52-Week Safety Study: VYZULTA Reduced Mean IOP to 14.4 mm Hg in Subjects with Mean Low Baseline IOP of 19.6 mm Hg

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Latanoprostene Bunod

- Reduces trabecular meshwork cell contractility and increases outflow compared with latanoprost
- May increase blood flow to the axonal bed

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When will we know if NO works?



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Alpha Antagonists

- Decreased action during sleep
- Topical reaction either immediate or delayed
- Somnolence risk
- Moderate miosis
- Good mono or adjunct therapy
- Possible neuroprotection



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Brimonidine dermatitis



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Carbonic Anhydrase Inhibitors

- Decrease in aqueous production
- Good 24 hour profile
- Possible profusion enhancement to axons
- Watch for sulfonamide sensitivity
- Sting with application
- Preservative free alternative
- Good mono or adjunct therapy
- Possible neuroprotection



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Beta Blockers

- Introduced mid 1970's
- QD vs. BID dosage
- Good adjunctive
- Cardiovascular risk
- COPD risk
- Lethargy / libido risk
- Poor action during sleep

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Beta Blockers

Are they all the same?



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Miotics

- Standard of care until mid 1970's
- Visual effects / miosis
- Retinal Detachment
- Cholinergic risk factors
- Special application with angles at risk



miosis



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Combinations

- Cost benefit
- Convenience benefit
- Compliance benefit



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Combinations

- Prostaglandin + beta blocker (not in U.S.)
- Alpha adrenergic + beta blocker
- CAI + beta blocker
- CAI + alpha adrenergic
- Prostaglandin + rho kinase inhibitor (3/2019 in U.S.)

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RHOPRESSA

(netarsudil ophthalmic solution .02%)
Aerie Pharmaceuticals, Inc.

(approved March 2018)

RHOPRESSA

(netarsudil ophthalmic solution .02%)

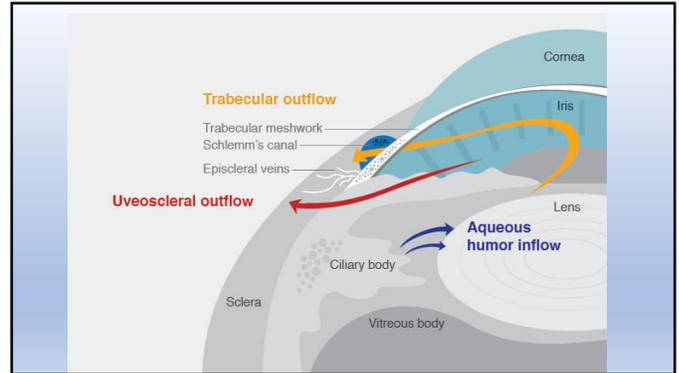
- Rho kinase inhibition ("ROCK" inhibitor)
- QD dosing
- Complimentary to prostaglandins
- Reduction of epi scleral venous pressure

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•Patients treated with once-daily **Rhopressa** experienced a reduction of IOP ranging from **3.9 mmHg to 4.1 mmHg⁴**

•Patients treated with twice-daily **timolol** experienced a reduction of IOP ranging from **3.5 mmHg to 4.6 mmHg**

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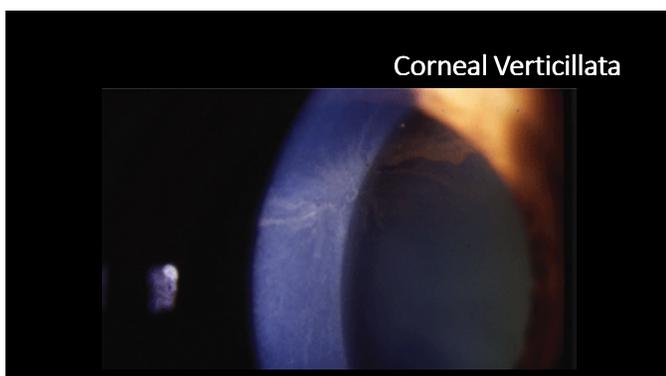
INTRO SAFETY EFFICACY COMMERCIAL COMPETITIVE LANDSCAPE RISK VALUATION

In ROCKET1 and ROCKET2, somewhere between 5% and 15% of patients encountered one or more of the following side effects

Corneal deposits Blurry vision Conjunctival hemorrhage

Wunderkind Research

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Rho Kinase Inhibitors

- First unique new topical glaucoma therapy since mid 1990's
- QD dosing
- Seems to perform best as an adjunct therapy
- IOP reduction in some patients to low teens
- Outflow via trabecular relaxation
- Significant hyperemia response
- Reduction of barrier of episcleral venous pressure

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Newest

- Rocklatan – rho kinase inhibitor + PGA
(approved 3/12/2019)



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generics

- Cost benefit
- Red tape benefit
- Compliance benefit

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Compliance / Generics

The University of Michigan research team examined patient medication-compliance patterns before and after latanoprost became available in 2011.

Patients who continued to use brand-name drugs (such as Xalatan) were 39 percent more likely to experience a decline in compliance, compared to those who switched to the newly-available and less expensive generic latanoprost

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Generic Prostaglandin Efficacy

- Can anyone cite a double blind randomized clinical trial which proves a significant decrease in efficacy with generic latanoprost?

?

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Compounding Pharmacies

- Almost all combinations possible!
- Imprimis Pharmaceuticals 858-704-4040

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Preservative Free Latanoprost 0.005% Available Now from ImprimisRx

AS LOW AS \$23 A MONTH*

Simple Drops Compounded Formulations**		
LAT Latanoprost 0.005% (Currently on FDA Shortage List)	7.5mL	\$99.00 (\$23.00 per month)
DOR Dorzolamide 2%	10mL	\$90.00 (\$20.00 per month)
TIM LAT* Timolol 0.5%/Latanoprost 0.005%	5mL	\$99.00 (\$49.00 per month)
BIM DOR* Brimonidine 0.15%/Dorzolamide 2%	10mL	\$110.00 (\$49.00 per month)
TIM BIM DOR* Timolol 0.5%/Brimonidine 0.15%/Dorzolamide 2%	10mL	\$159.00 (\$79.00 per month)
TIM DOR LAT* Timolol 0.5%/Dorzolamide 2%/Latanoprost 0.005%	5mL	\$110.00 (\$59.00 per month)
TIM BIM DOR LAT* Timolol 0.5%/Brimonidine 0.15%/Dorzolamide 2%/Latanoprost 0.005%	5mL	\$159.00 (\$79.00 per month)

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orals

- Acetazolamide – for acute treatment
- 500 mg – with acute attack then 250 QID
- Watch for sulfonamide allergy, dehydration, lethargy

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orals

- Methazolamide - for chronic treatment
- 50 mg BID
- Watch for dehydration, lethargy

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Surgery

- SLT
- MIGS
- Endo-cyclo-photo-coagulation (ECP) | Eye Surgery
- Tubes / Trabeculectomy

The slide contains several diagrams and images illustrating surgical techniques. At the top left is a close-up of a laser procedure. In the top center is a diagram of a MIGS device with labels: Scleral, Isthm, Trabecular Meshwork, and Soft Enabling Tip. To its right is a diagram of the eye's drainage angle with a green arrow indicating laser treatment. Below these are three more images: a purple laser probe, a diagram of a tube shunt with labels (Isthm, Sclera, Trabecular Meshwork, Soft Enabling Tip, and Scleral Flap), and a photograph of a surgical procedure on an eye.

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compliance

- Realistic assessment of patient
- Non confrontational doctor patient communication
- Cost and accessibility considerations
- Drop application

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Stick to the 3 critical points in management

Fields →

Nerves →

Pressures →

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treatment goals

Reduce IOP and enhance perfusion to halt or minimize progression in the safest and most economical and energy efficient manner

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monocular clinical trials?

don't

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monocular treatment

don't

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under treatment
late treatment

don't

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Delay follow up visits?

don't

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Be AFRAID to add medicine?

don't

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Be AFRAID to use combination drugs as monotherapy?

don't

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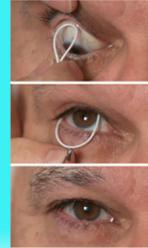
Forget oral medications

don't

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Sustained Release Preparations

- **Bimatoprost Ocular Ring** – *Allergan*
- thin silicone ring suffused with bimatoprost
- slowly releases drug over a 6 month period



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Sustained Release Preparations

- **Bimatoprost SR Implant** - *Allergan*

A Biodegradable device that is implanted intracamerally with a preloaded single use injector which slowly releases Bimatoprost over months



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Sustained Release Preparations

- **The iDose** – *Glaukos*
- A titanium implant implanted in similar fashion to an iStent
- The implant is filled with a formulation of travoprost specific to the device and capped with a membrane designed for continuous controlled drug elution into the anterior chamber.
- When the medication has been exhausted, the implant can be removed and replaced in the same minimally invasive fashion.



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Sustained Release Preparations

- **Travaprost Punctal Plugs** – *Ocular Therapeutix*
- Bioabsorbable plug made of polyethylene glycol hydrogel that releases travaprost as it degrades



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Sustained Release Preparations

- **TODDD (Topical Ophthalmic Delivery Device)** – *Amorphex Therapeutics*
- Made of a biocompatible soft elastomeric material
- sits on the surface of the sclera underneath the eyelid
- tested various drops individually and as a combination, including timolol maleate, prostaglandins, pilocarpine, brimonidine
- even some anti-inflammatories and antibiotics.



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Non Traditional Therapies

- Attention to blood pressure – Diastolic Perfusion Pressure
- Hydration and salt
- Ginkgo - biloba?

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COST

- Coupons vs. Generics



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the right recipe

- Glaucoma therapy requires an ongoing effort to find and adjust the most acceptable therapy (recipe) for each individual



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Thank You!

Elliot M. Kirstein, OD, FAAO

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Cincinnati, Ohio

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